COMPUTERIZED IMAGE ANALYSIS OF SONOGRAPHIC BREAST LESIONS

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A goal of the proposed research was to develop noninvasive, computerized methods for analyzing ultrasound images of breast lesions to aid radiologists in their workup of suspect lesions. The specific objectives of the research to be addressed including creating adatabase with known pathology of breast lesions on sonography, developing computerized methods for the automated segmentation and automated characterization of lesons on sonography, and evaluating the the new methods in the task of distinguishing between malignant and benign lesions. It is expected that the results from this research will aid radiologists in determining the likelihood of malignancy and in reducing the number of benign cases sent to biopsy.

The overall computerized classification method for mass lesions on sonograms include: (1) automatic lesion extraction, (2) automated feature extraction, and (3) automatic classification for merging the features into an estimate of the likelihood of malignancy. We evaluated our computerized sonographic lesion analysis method on a database of ultrasound images. Of the 410 cases, 126 were complex cysts, 186 were benign solid lesions, and 98 were malignant lesions. Features related to lesion margin, shape, echogenicity (texture) and posterior acoustic attenuation are automatically extracted. To evaluate the performance of the computer alone, the entire database was divided into training and testing groups. The independent linear discriminant analysis yielded a validation result of an Az of 0.89 and a partial Az value at 0.90 sensitivity of 0.52. In addition, in order to evaluate the performance of the computer relative to that of the radiologists, 125 cases were assessed for suspicion by an expert sonographer. Round-robin analysis in the task of distinguishing malignant from benign lesions yielded Az values of 0.88 and 0.92 for the computer and the radiologist, respectively.

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A NEW MODEL FOR THE ESTIMATION OF BREAST CANCER RISK

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Cancer risk is the probability that cancer will occur in a given population. Research on cancer risk seeks to identify populations with a high probability of developing cancer. The goal of this research was to develop a novel model for use in estimating risk of breast cancer. Potential uses of this innovative model include 1) serving as a means to assess the cancer risk of women undergoing routine screening mammography and thus, identifying those women that may require closer scrutiny and 2) serving as a means to monitor the cancer risk of women undergoing chemoprevention treatments.

In our studies, we identified computer-extracted, mammographic parenchymal patterns that are associated with breast cancer risk. We extracted fourteen features from the central breast region on digitized mammograms to characterize the mammographic parenchymal patterns of women at different risk levels. In one study, the features were used to characterize mammographic patterns seen in low-risk women and in women who have breast cancer. Stepwise linear logistic regression was employed to identify useful features to differentiate between the mammographic patterns of low-risk women and women with breast cancer. The relationship between these mammographic patterns and the risk of developing breast cancer was identified based on the odds ratios associated with these individual features. We also employed two other approaches to relate these mammographic features to breast cancer risk. In one approach, the features were used to distinguish mammographic patterns seen in low-risk women from those who inherited a mutated form of the BRCA1/BRCA2 gene. In another approach, the features were related to risk as determined from existing clinical models (Gail and Claus models). Stepwise linear discriminant analysis was employed to identify features that were useful in differentiating between "low-risk" women and BRCA1/BRCA2-mutation carriers. Stepwise linear regression analysis was employed to identify useful features in predicting the risk as estimated from the Gail and Claus models. Results from all three approaches indicate that women who have dense breasts and whose mammographic patterns are coarse and low in contrast have an increased risk of developing breast cancer.

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AUTOMATED REGISTRATION AND CHARACTERIZATION TECHNIQUES FOR INTERVAL CHANGE ANALYSIS IN MAMMOGRAPHY

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The goal of this project is to develop a computer-aided diagnosis (CAD) system for interval change analysis of lesions on mammograms. The CAD system includes two stages: automated registration of corresponding lesions on temporal pairs of mammograms, and classification of the lesion as malignant or benign using interval change information.

A regional registration technique was developed for identifying corresponding masses on temporal pairs of mammograms. An initial fan-shape search region was defined on the prior mammogram based on the mass location on the current mammogram. The location of the search region was refined by warping using affine transformation in combination with simplex optimization. A search for the best match between the lesion template from the current mammogram and a structure on the prior mammogram was carried out within a search region, guided by an adaptive similarity measure. This new approach was evaluated by using 179 temporal pairs of mammograms containing biopsy-proven masses. It was found that 86% of the estimated lesion locations resulted in an area overlap of at least 50% with the true lesion locations. The average distance between the estimated and the true lesion centroids on the prior mammogram was 4.5 ± 6.7 mm.

A new classification scheme was developed for characterization of mammographic masses using interval change information. The masses on both the current and the prior mammograms were automatically segmented using an active contour model. From each mass, texture, spiculation and morphological features were extracted. Difference features were obtained by subtracting the prior from the corresponding current features. Stepwise feature selection and linear discriminant analysis classification were used to select and merge the most useful features. A leave-one-case-out resampling scheme was used to train and test the classifier using 140 temporal image pairs (85 malignant, 55 benign) obtained from 57 biopsy-proven masses (33 malignant, 24 benign) in 56 patients. The classifier achieved an average training A_z of 0.92 and a test A_z of 0.88.

Our studies indicate that an accurate automated method can be developed for interval change analysis. Computer-aided interval change analysis is expected to be useful for improving breast cancer diagnosis and reducing unnecessary benign biopsies.

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SPECTRAL ANALYSIS OF FULL-FIELD DIGITAL MAMMOGRAPHY DATA: IMPLICATIONS FOR AUTOMATED MAMMOGRAPHIC DENSITY LABELING AND MASS DETECTION

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In the work presented here the spectral analysis of full field digital mammography (FFDM) data is discussed. The spectral analysis forms the basis for automatically labeling dense tissue; dense tissue is generally accepted as an important breast cancer risk factor. In addition, the density labeling may be considered as the first step in devloping a mass detection method. The image data are acquired with the General Electric Senographe 2000 D FFDM system with 14-bit pixel accuracy at 100μm digital resolution.

Previous work in digital mammography indicates that mammograms may be considered as evolving from a linear filtering process. First, the form of the filter is approximated with Fourier domain modeling methods. This is followed by a deconvolution technique applied to the raw image, which produces the input field to the assumed filtering process. This field has a frequency spectrum that is roughly flat or constant. Applying chi-square statistical analysis to this field allows for the automated discrimination of dense tissue from non-dense tissue. This follows from assuming that two tissue modes exist, one for fatty tissue and the other for dense tissue, differing only by the associated probability distribution variances. The spectral analysis of 100 images indicates that FFDM obey inverse power law; that is the frequency power spectrum drops off as $1/f^{2\alpha}$ with $\alpha \approx 1.4\text{-}1.5$.

Applying the technique to the raw FFDM data resulted in a density labeling that was less than optimal. This problem was addressed by applying a non-linear transform to the raw data prior to the density analysis. Preliminary evidence indicates that the performance, following the transform, was similar to that obtained when applying the technique to digitized film data. The transform is based on standardizing the FFDM data to that of the digitized film data, which was analyzed previously. In 85% of the cases where masses were present, the density labeling also marked the mass areas as well.

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NORMAL TISSUE IDENTIFICATION AT SCALES RELEVANT TO CALCIFICATIONS IN FULL-FIELD DIGITAL MAMMOGRAPHY

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In the past, computer aided diagnosis (CAD) methods have been applied to digitized film images with the aim of improving screening sensitivity and specificity rates in mammography. More recently full field digital mammography (FFDM) has gained acceptance and is in operation at a limited number of facilities. FFDM is a film-less mammography system, where the images are acquired in digital format. FFDM has the potential to facilitate many teleradiology applications. In the regular mammographic screening environment, the vast majority of images are normal at any given time. Moreover, even when an image is declared abnormal the vast majority of breast tissue is normal. A method of detecting clinically normal images may be very useful. Here we discuss the results of applying normal image recognition techniques to FFDM data. The image data, consisting of 100 images, are acquired with the General Electric Senographe 2000 D FFDM system with 14-bit pixel accuracy at 100μm digital resolution. Half of the images lack identifiable clusters and 50 images have at least one cluster.

The approach is based on modeling normal tissue at scales relevant to the anticipated abnormality. Here we use the presence of calcified areas (small-scale) as the definition for abnormality and leave larger scales relevant to masses for future work. First the area of the image that contains the breast is determined and the image is band-pass filtered, which isolates the relevant scales. Here the background area implies the breast signal, which is not calcified. Empirical evidence indicates that the relevant bandwidth is roughly 3.15 ± 0.5 cycles/mm. A small search window is scanned across the image (first stage detection) constrained to the breast region. Based on summary statistical analysis, when an area meets the definition for normal it is set to zero, otherwise it is assumed suspicious. As a further measure to reduce the number of normal regions labeled as suspicious, a larger box ($1 \text{ cm} \times 1 \text{ cm}$) is scanned across the image. When a larger region lacks less than three isolated abnormal smaller regions it is set to zero.

The detection analysis shows it is possible to detect 94% percent of the verified clusters. However in order to gain this sensitivity, the false positive (FP) cluster rate is 3.7 clusters/image. Although the normal tissue modeling permits acceptable sensitivity rates, more work is needed to reduce the FP rate. As a further FP reduction measure, a logistic regression model was applied to the first stage detection output, where the multiresolution power was used as the model parameters, which allows an 88% detection rate with 2.75 FPs/image.

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COMPUTER-AIDED DIAGNOSIS OF MALIGNANT AND BENIGN BREAST LESIONS IN MAMMOGRAMS

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The diagnosis of malignant and benign breast lesions in mammograms often requires a biopsy that, in turn, results in a large number of benign lesion biopsies. Previously, we developed computer methods that classify breast lesions as malignant or benign based on computer-extracted image features independent of radiologists' interpretation of the mammogram. These computer methods have been shown to be highly accurate and able to improve radiologists' diagnostic accuracy. The purpose of the present investigation is to improve the computer methods by incorporating radiologists' identified lesion features and by combining the computer and radiologists' assessments of the lesion in a theoretically "optimal" way.

We used a mammogram database of 166 breast lesions (67 mass or architectural distortion and 99 microcalcification lesions) that included standard-view and magnification- or spot compression-view mammograms. Volunteer experienced mammographers read the mammograms and provided (1) BI-RADS lesion descriptions, and (2) an estimate of the likelihood of malignancy. The lesion descriptions were then used as input to the computer classification methods and the computer classification accuracy was compared when computer-extracted image features alone were used as input versus when the BI-RADS lesion descriptions were added as input. Finally, the computer and the radiologist's estimate of the likelihood of malignancy were combined using a model that we have developed.

Classification accuracy of the computer methods improved when the BI-RADS lesion descriptions were used as input in addition to the computer-extracted image features. For mass lesions, the area under the ROC curve (Az) increased from 0.73 to 0.96. For microcalcification lesions, Az increased from 0.73 to 0.75. Combining the computer and the radiologists' diagnostic assessment resulted in higher Az values.

These results indicate that computer classification of malignant and benign breast lesions in mammograms can be further improved. Computer-aided diagnosis can potentially help reduce the number of benign lesion biopsies, thereby improve the effectiveness of mammography screening for breast cancer.

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DETECTION OF MASSES IN MAMMOGRAPHY THROUGH REDUNDANT EXPANSIONS OF SCALE

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We show that dyadic scales may not be sufficient for the detection of masses in mammograms: a lesion may be too blurred on one scale, while too fragmented at the next larger scale. In this paper, we report on preliminary results of our study using a continuous wavelet transform in two dimensions where arbitrary positioning of a wavelet's center frequency channel allows us to "tune" the analysis to a particular size of a mass for detection. Our goal is to detect masses in dense mammograms whose diameter is smaller than 1 cm. Our near term aim is to be able to automatically find the scale where a mass is best represented in terms of analysis.

An initial study in one dimension led us to observe that dyadic scales of expansion are often not sufficient to detect a mass in dense mammograms. In this early study, a continuous wavelet transform computed the decomposition on voices between traditional dyadic scales. We showed that it is possible to expand a signal more finely and compute scales between octaves of traditional dyadic expansions by voices. A voice constitutes a subdivision of an octave. We observed on masses extracted from digitized clinical mammograms a maximum correlation between a known mass and the values of computed analysis coefficients. Thus, this study suggests that it is indeed possible and of potential clinical value to tune an analysis between octaves, for the detection of subtle masses in mammograms.

More recently we have focused on computing fractional spline wavelets (FSW). We have extended its original 1D implementation (Unser and Blu), to two-dimensions for the analysis of masses. The transform was computed for selected samples of clinical masses along scales for different values of the spline parameter alpha, which changes the shape of the spline basis. This study allowed us to vary the spline parameter in order to find the basis which best matches a given mass size. With such a continuous analysis, we were able to construct a richer parameter space in which to identify a best basis for the detection of subtle masses.

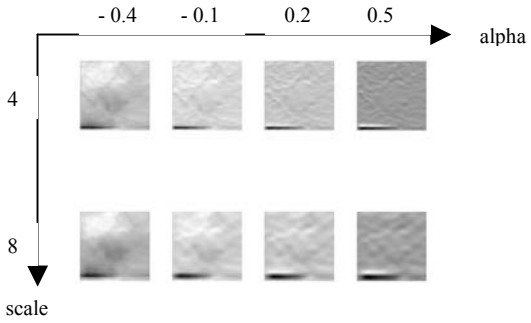

Figure 1. Analysis coefficients of a 2D FSW at scales 4 and 8, for four values of the spline parameter α.

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IMPROVING ALGORITHM ROBUSTNESS FOR MASS DETECTION IN DIGITAL MAMMOGRAPHY

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Computer aided diagnosis (CAD) has been proposed as a low cost and efficient approach to improve mammographic imaging and interpretation. There are several examples in the literature of increasing lesion detection through the use of CAD methods. However, one significant limitation of CAD studies is that a computerized method may be developed and evaluated on a database comprised of a limited number of selected cases. The performance of the CAD method may highly depend on the subtlety of the lesions and have a great variation for different mammograms taken at different site and/or time. The purpose of this study is to develop a robust CAD mass detection method, which has a good detection performance and generalizability.

The typical variations between different mammograms may result from the imaging process, digitization process (for screen-film mammography), or the inherent breast tissue characteristics. The variation of masses includes its size, contrast, shape, margin, location, intensity pattern and its relation to the surrounding tissues. The proposed CAD mass detection method is a modification of our first generation wavelet based detection method. It addressed the variation problems by using adaptive, multi-scale processing and hybrid classification strategies. Specifically the major techniques developed in system design include (a) image standardization by applying a series of preprocessing to remove extrinsic signal, extract breast area, and normalize the image intensity values; (b) multi-mode processing by image feature decomposition using directional wavelet transform (DWT) and non-linear multi-scale representation; (c) adaptive processing in image segmentation using a localized adaptive thresholding and adaptive clustering (AC); and (d) combined "hard"-"soft" classification by using a modified fuzzy decision tree and competitive classification method.

The CAD mass detection method was tested using two independent testing databases. The results demonstrated that the new method has a better detection sensitivity/specificity and a much better robustness. The difference of detection sensitivity on two testing databases is as little as 1% for the new method as opposed to 12% for the old method both at a similar false positive rate.

A new method was presented to improve robustness of mass detection in mammography. This research is very important because a CAD method can be applied in practice only when it has a good performance and generalizability.

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COMPUTER-AIDED ALGORITHMS FOR BREAST TUMOR DIAGNOSIS USING MICROWAVE DIFFRACTION MEASUREMENTS

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Introduction – The purpose of this research is to use signal detection theory to improve the performance in detecting breast tumor. It is used to develop task oriented information processing techniques that use microwave diffraction measurements, and that address directly the decision-theoretic task of detection, localization and classification of the tumor as malignant or benign. This improvement in performance is possible because conventional imaging techniques, by themselves, usually emphasize resolution and contrast, and leave the incorporation of uncertainties and decisions primarily to algorithms or human observers that post process the reconstructed image. This approach augments conventional medical image processing and provides additional processing of the scattered microwave field to aid the radiologist in dealing with uncertainties that are an inherent part of the decisions.

Brief description – Sha et al have compiled results from experiments in the literature that show that the microwave dielectric properties of malignant tissue is different from that of normal breast tissue. Signal detection theory, in its most fundamental form, provides a framework for incorporating this knowledge of breast tissue characteristics directly into the design of optimal task oriented information processing algorithms to aid in the detection of breast cancer. In addition, signal detection theory enables one to obtain upper limits of detection and localization performance as a function of uncertainties in the microwave properties of breast tissues, using quantitative measures such as the ROC (probability of detection vs. false alarm) and PCL (probability of correct localization). The optimal algorithm uses the direct microwave diffraction measurements and incorporates the fact that spatially adjacent tissues are similar in their permittivity values, but normal and malignant breast tissues have high contrast in the mean. The microwave diffraction measurements are computed using the Extended Born Approximation (EBA) accelerated CGFFT method[1] with an ensemble of simulated breast permittivity images as the propagating media.

Summary of results to date – Using the ROC and PCL performance measures and simulation, the best tumor detection and localization performance for microwave imaging is shown as a function of tumor contrast, tumor size, tumor mean function and tumor local characteristics. Also, the performance of the optimal statistical decision based algorithms is compared to ones that post process reconstructed images of breast permittivity[2]. These results demonstrate the advantages of incorporating the microwave diffraction measurements directly into the computer-aided algorithm design.

Conclusion – Microwave energy has the advantages that at the low power levels there are no radiation dangers, there are no contrast agents, and the examinations are comfortable. Computer-aided breast tumor diagnostic algorithms based on microwaves and signal detection theory has the potential of providing additional information for radiologists so as to improve the probability of detection of breast tumors as well as their correct localization.

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DETECTING BREAST CANCER FROM THERMAL INFRARED IMAGES BY ASYMMETRY ANALYSIS

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This project started in August, 2001. It is a research effort that helps define thermal infrared (TIR) imaging as a diagnostic tool in early detection of breast cancer, which can be used as a complementary to traditional mammography.

Research has shown that if detected earlier (tumor size less than 10mm), the breast cancer patient has an 85% chance of cure as opposed to 10% if detected late. TIR imaging, as a non-invasive, non-ionizing imaging modality, can provide functional information about the cancer cell that is not easily measured by other methods like X-ray radiology and CT that primarily provide information on the anatomical structures.

TIR images the heat emanating from the heat source, transported by the radiation and picked up by the Infrared (IR) on the surface. Cancerous tissue absorbs 5 – 10 times more glucose and liberates less energy than the normal cells. The high metabolic activity keeps the cancer cell at a higher temperature than the normal cell. Therefore, tumors of the breast induce abnormalities in skin temperature which can be detected by TIR.

One of the popular methods for breast cancer detection is to make comparisons between contralateral images. When the images are relatively symmetrical, small asymmetries may indicate a suspicious region. In TIR imaging, asymmetry analysis normally needs human interference because of the difficulties in automatic segmentation. In order to provide a more objective diagnosis result, we propose an automatic approach to asymmetry analysis in thermograms. It includes automatic segmentation and supervised pattern classification. Hough transform is used to extract the four feature curves (the left and right body boundaries and the parabolic-shaped lower boundaries of the breasts) that uniquely segment the left and right breasts. Upon segmentation, statistical features (moment measurements of the local histogram) are derived from both segments. Ratios between the corresponding feature values from each segment are used as inputs to the supervised learning methods (k-Nearest-Neighbor and Maximum Posteriori Probability) for classification.

Experiments have been conducted based on images provided by Elliott Mastology Center (Inframetrics 600M camera) and Bioyear, Inc. (Microbolometer uncooled camera).

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AN OPTIMIZED CAD SYSTEM FOR MCCS DETECTION IN DIGITAL MAMMOGRAPHY FOR MULTICENTER REMOTE DIAGNOSIS

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The aims of this work are to explore the feasibility of developing a *new class* of computer assisted diagnostic (CAD) methods for microcalcifications cluster (MCC) detection for remote breast cancer screening using digital mammography. The objectives are to achieve: (a) improved CAD performance that is significantly more robust for large image data bases, and (b) an *adaptive* CAD method that is independent of the digital sensor resolution and gray scale characteristics; for the first time. This paper includes 2 sections, **(1). Summary of the work in past year, which includes data base collection and truth file establishment for different sensors, preprocessing for breast area segmentation, and basic algorithm design, (2). Algorithm design and optimization for multi-center remote diagnosis,** which includes a design of a successful MCCs detection system containing the design and optimization of all modules. Some detail of our progress is summarized in our recent publications [1, 2, 3, 4, 5]. *A CAD method with improved and robust performance is required for both retrospective studies and an steps towards a more generalizable CAD method, which is critical for multi-center clinical trials.* The proposed method is novel in concept and is based on pioneering experience in development of adaptive CAD algorithms including linear wavelet transforms and non linear transforms for improved feature extraction, their implementation of filter banks that uniquely allow adaptive approaches, and experience in specialized multi-stage neural networks for detection of MCC's with different feature input strategies. The intent is to compare existing wavelet methods to the proposed new method and evaluate them for a *common case* database using a state of the art direct digital detector and film (three digitizers).

The research efforts involve design and optimization of all CAD modules. We first implemented a robust CAD module of breast segmentation, already developed, that is generalizable to different sensors, a modification of a reported method. We then focused on the design and optimization of nonlinear filter banks based methods for MCC enhancement. This should be optimized to maintain a high detection sensitivity and low false positive rate. A CAD module for MCC identification criteria, which is an extension of previous work, should be modified for more accurate cluster extraction from binary images. Extraction of explicit features (inter-projection) should be greatly emphasized and as extension of our work on implicit features . Existing multistage based NN methods will still be adopted and optimized by using input both implicit and explicit features at different stages.

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COMPUTERIZED ANALYSIS OF SOLID MASSES IN 3D ULTRASOUND VOLUMES FOR BREAST CANCER DIAGNOSIS

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The overall goal of this research is to develop computer vision techniques for analysis of multi-modality images of breast masses to improve the radiologists' accuracy in biopsy recommendation. The specific goal of this study was to develop automated methods for characterizing masses on three-dimensional (3D) sonograms. The sonographic image analysis can be combined with mammographic analysis to improve the accuracy of differentiating malignant and benign masses.

The 3D image acquisition system consisted of a commercially available ultrasound scanner (GE Logiq MR 700 with a M12 array transducer) and a mechanical transducer guiding system. The 3D volumes were recorded by translating the transducer across the lesion in the z-direction while conventional 2D images were acquired in the x-y plane. A 3D image segmentation method based on an active contour model was developed to delineate the mass boundaries. Using the segmented mass shape, features that described the width-to-height ratio and the texture of the interior and along the margin of the lesion, as well as its attenuation were extracted. A feature classifier was designed using the leave-one-case-out method to combine the features into a malignancy score and to estimate the classification accuracy. The classifier scores were analyzed using the Receiver Operating Characteristic (ROC) methodology.

To date, 3D volumes containing solid breast masses with biopsy-proven pathology have been acquired from over 90 patients, and 51 of these cases (29 benign and 22 malignant) have been analyzed with our computerized classification method. The classifier achieved an area under the ROC curve of 0.92. More than 30% of the benign masses in this data set could be correctly identified using the classifier scores without missing a malignancy. These results show the promise that an accurate computer classifier can be designed for differentiation of malignant and benign solid breast masses on 3D sonograms. Combination of sonographic and mammographic computer image analyses can provide radiologists with a powerful tool for decreasing the number of benign biopsies without reducing the sensitivity of cancer detection.

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DATABASE-AIDED DETECTION AND DIAGNOSIS OF MAMMOGRAMS

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We devised, constructed and tested a computer-supported system that enables radiologists to interact efficiently with a large database of biopsy-proven, benign-tracked mammographic images. The principal objective of this system is to aid radiologists' performance in the detection and diagnosis of breast abnormalities. Toward this objective our system provides the following benefits:

1. The radiologist has control over image enhancement, databases, and scoring.
2. Normal breasts and benign lesions are classified by our system as benign with high reliability.
3. The radiologist can search databases for cases similar to the presented case.
4. The radiologist can access remotely sited databases at high speed.

The system includes a detector of abnormal lesions and a detector of regions of suspicious abnormalities. The detector is designed to suppress a large percent of normal breasts. The detector is coupled to a classifier that is designed to suppress falsely detected lesions. The system includes high-resolution digital displays of both full mammograms and detected regions of interest, and a search engine for accessing remotely sited databases.
The radiologist participates in the selection of the regions of interest. The basic elements of this system include a database of over 1000 proven mammographic cases, a patented neural network that maps all of these cases into a "relational" map, and a novel detector of filamentary structures in normal breast images. The relational map displays similar cases as clusters of points, each point representing a single mammographic examination. These similar cases help the radiologist to suppress false positives.

We describe the basic organization and performance of our database-aided system and its essential elements. And we describe a retrospective test of our system on over 500 proven cases acquired from the UCLA School of Medicine and the Charles R. Drew University of Medicine & Science. The test is carried out by a panel of six radiologists certified for mammography. We also compare our diagnostic system as a second reader for remote diagnosis of mammograms by a human expert reader. In the remotely diagnosed system, the images are transmitted over a 7-mile dedicated T1 line to the King/Drew Medical Center from the Hubert H. Humphrey Comprehensive Health Center. The results include an evaluation of the ability of our system to help reduce the number of false positives without increasing the number of missed cancers.

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TACTILE MAPPING AND TUMOR MODELING FOR BREAST CANCER DETECTION

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This project presents the development of a Tactile Mapping Device (TMD) system prototype comprised mainly of a tactile sensor array probe, a 3D camera and a force/torque sensor, which can provide the means to produce tactile maps of the breast lumps during a breast palpation. Focusing on key tactile topology features from breast palpation such as spatial location, size and shape of the detected lesion, and the force levels used to demonstrate the palpation abnormalities, these maps can record the results of clinical breast examination with a set of pressure distribution profiles and force sensor measurements due to the detected lesion. By combining the knowledge of vision based neural networks, tactile sensing technology is integrated for the investigation of soft tissue interaction with tactile/force sensor, where the hard inclusion (breast lump) can be characterized through neural network learning capabilities, instead of using a simplified complex biomechanics model with many heuristic assumptions. These maps will serve as an objective documentation of palpable lesions for future comparative examinations.

In addition to the tactile mapping evaluation by breast palpation, we propose to incorporate tumor modeling of breast MR sequences, with a goal of estimating and tracking changes of the simulated and/or real tumor across time. Based on the breast MR datasets, we can construct an MR model of a tumor to detect changes over time. The method is to apply the segmentation algorithm to extract the tumor regions from the sequence of breast MR images. Once the tumors have been extracted, we can estimate the volume of the tumor in terms of the size and shape of the tumor. Furthermore, we can estimate the quantitative change in the volume of the tumor across time. The proposed method will not only help the physician in the documentation of the detected lesions by TMD, it can also help to better the understanding of how a tumor progresses after the initial palpation has been detected.

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SYSTEM-ORIENTED OPTIMIZATION OF COMPUTER-AIDED DETECTION (CAD) FOR MASS DETECTION ON DIGITAL MAMMOGRAM

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The purpose of this work is to improve the overall performance of computer aided-detection (CAD) system for mass detection on digital mammograms. It aims at the development of a new kind of fully optimized CAD system using system oriented optimization algorithm. The specific aims of current work include: (1) design of new algorithms for CAD system, (2) development of adaptive modules, (3) the configuration of CAD system optimization system using adaptive simulated annealing (SA) algorithm.

New methods have been developed and adaptive modules have been modified for CAD system. To image preprocessing module, adaptive tree-structured filtering (TSF) module has been developed for noise suppression. Adaptive tree-structured wavelet transform (TSWT) module and adaptive directional wavelet transform (DWT) module have been developed respectively for image enhancement. Adaptive fuzzy C-means module has been designed and adaptive clustering (AC) segmentation method has been modified for segmentation module. In classification module, feature ranking and selection has been modified adaptively, the artificial neural network (ANN) classifier has also been designed adaptively including the configuration of ANN and its training algorithm.

The CAD optimization system has been constructed using adaptive simulated annealing algorithm. Due to the cascade characteristic of CAD modules in cancer detection, its performance is dependent on many parameters with different type, while empirical parameter setting or fixed is not available to make the system robust or efficient. Furthermore, the optimization of such complicated system is obviously a typical combinatorial mixed-discrete optimization due to the combination of different types of design variables. Adaptive simulated annealing (SA) algorithm is employed for the system optimization and integrated with CAD system. Several variables with different types are chosen as optimization variables.

The CAD system is initially optimized on a training database and evaluated using a testing database. The training and the testing database contain 60 cases and 120 cases, respectively. All cases are biopsy proven and generated ground truth by experienced radiologists. A series of case selection criteria has been followed in the construction of these two databases. The sensitivity and false positive (FP) rate for the optimized CAD system are 83% and 3.1/masses per image respectively compared with 74% and the FP rate of 4.8 masses per image respectively on the corresponding un-optimized system on the same testing database.

The obvious CAD system performance improvement has been observed through system-oriented optimization with adaptive SA algorithm on current testing database. It expresses the feasibility and efficacy of proposed method for CAD system performance improvement on mass detection. Not only providing a reasonable parameter matching method for different modules in CAD system, but also this research work will develop an efficient and robust CAD system for mass detection that can be for clinical trial.

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A CONSTRAINT SATISFACTION NEURAL NETWORK FOR DATA MINING A BREAST CANCER DATABASE

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The purpose of this study was to explore the Constraint Satisfaction Neural Network (CSNN) as the basis for a decision support system to assist pphysicians in the clinical recommendation to biopsy suspicious, non-palpable, breast lesions that remain unresolved after a diagnostic mammogram.

The study is based on the hypothesis that a patient can be modeled as a non-linear, dynamic system comprised of several components (e.g., clinical and history findings, mammographic findings, presence or absence of breast cancer). All components are coded into variables interconnected with constraints to keep the system stable. Typically, there is information about some system components (e.g., mammographic findings) and some questions need to be answered (e.g., Is there breast cancer?). Answering such questions is equivalent to finding the optimal values for the corresponding variables (i.e., lesion malignancy) so that the system constraints are satisfied to a maximum extent and the system is stable. The CSNN is a dynamic, non-hierarchical network designed to solve this type of system optimization problem.

The CSNN was developed and evaluated using a database of 1,530 non-palpable breast lesions with definitive histopathological diagnosis. Complete mammographic and clinical findings were available for 848 patients. For the remaining 682 patients, there were only mammographic findings available. Initially, the CSNN was developed and evaluated on the 848 complete patient files using the 50%-50% cross-validation sampling scheme and Receiver Operating Characteristics (ROC) analysis. The CSNN had an overall ROC area index of 0.83±0.03. The CSNN was further validated on the 682 patients with incomplete findings showing an ROC area index of 0.77±0.03. The CSNN predictive performance was competitive with that achieved by experienced radiologists and a backpropagation neural network. Furthermore, the study illustrated how the CSNN can be used as a flexible knowledge discovery tool to describe data trends and hidden associations related to its decision making process.

The immediate benefit of this study is a flexible, reliable, and interpretable decision support system that could reduce the economic, physical, and emotional cost associated with benign biopsies.

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IMPROVING CLINICAL DIAGNOSIS THROUGH CHANGE DETECTION IN IMAGE SEQUENCES

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Temporal change of mass lesions overtime is a key piece of information in computer-aided diagnosis of breast cancer and treatment monitoring. For a specific patient, change detection is a critical step to select lesion candidates for follow-up diagnosis performed by either clinicians or computers. In this project, we developed a hybrid image registration technique to align temporal sequences of the same patient and detect changing lesions, and developed a neural network based classifier to derive the probabilities of true masses.

In particular, we developed (1) mPAR and MLP based registration algorithm to recover non-rigid deformation; (2) a new change detection scheme using independent component analysis of image sequences; (3) a feature extraction algorithm to obtain discriminative imagery features of true masses against mass-like normal tissues; and (4) a neural network based decision support system for mass detection. Our preliminary studies have shown a very good performance of the mass detection system consisting of 91 mammograms. The performance was initially 0.78-0.80 for the areas Az under the ROC curves using the conventional neural network, and later being improved to Az values of 0.84-0.89 when using the newly developed multiple circular path neural networks.

At technology aspect, we describe the theoretic roadmap of least relative entropy matching of two point sets. The novel feature is to align two point sets without needing to establish explicit point correspondences. The recovery of transformational geometry is achieved using a mixture of principal axes registrations, whose parameters are estimated by minimizing the relative entropy between the two point distributions and using the expectation-maximization algorithm. We give evidence of the optimality of the method and we then evaluate the algorithm's performance in both rigid and non-rigid image registration cases.

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COMPUTER-AIDED EARLY DETECTION OF AXILLARY METASTASES WITH DYNAMIC PET

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Objectives: An accuracy of 85% for tumor detection can be achieved in the axilla of patients with breast cancer with the static PET-FDG images. However, an inaccuracy rate as high as 15% is not acceptable for replacing invasive axillary lymph node dissection. This project studied the feasibility of improving lesion detectability by exploiting the difference (tumor and normal tissue) and the similarity (primary tumor and metastasis) of physiological features via the kinetic parameter quantification and statistical detection.

Methods: Based on a PET-FDG three-compartmental (4K) model, the kinetic parameters are estimated from the known normal tissues, primary tumors, and metastases in the attenuation corrected clinical images. The nonlinear parameter estimation with the Newton-Raphson method, the FADS, and the spectral analysis were used for estimating the kinetic parameters. The estimated parameters were categorized into parameter subregions in a 4-dimensional real space R4 according to tumor types (lung and breast) and tissue types (normal tissue, primary tumor, and metastasis). Three statistical detection criteria were developed and compared to test which parameter subregion best characterizes an observed time activity curve. The first criterion assumed no spatial correlation between pixels in an ROI. The second taken the spatial inter-pixel correlation into account and pre-whitened the data with the covariance matrices computed frame by frame, based on Huesman's analytical formulas and Carson's simplifications. The third modeled that the spatial inter-pixel correlation in the i^{th} frame has the form $\sigma_i R$, i.e., each frame has the same spatial correlation structure R, but a different energy lever σ_i. Thus, the covariance matrix computed in the least noisy frames can be used as matrix R for noisier frames. The resulting test statistic consolidates the dynamic images into a single image for a computer-aided diagnosis.

Results: We used 50 sets of dynamic phantom simulations with/without artificially inserted lesions and also inserted artificial lesions into 20 sets of normal lung and breast dynamic clinical images from an ECAT953 scanner. These lesions were assigned clinically measured TACs of malignant lung and breast tissues, respectively. Results: Method 3 increased specificity and accuracy by 20 and 11%, respectively, compared to the other two methods. No significant difference was observed between Methods 1 and 2, which could be due to inaccurate covariance matrix estimation introduced by the simplifications made in the early frames. Data from 16 patients (8 lung and 8 breast cancers) were also tested for the study. Results: The method detected 7 metastases not visualized on standard attenuation corrected FBP images, 3 of which have been verified by a follow-up study acquired about 1.5 years later.

Conclusion: The sensitivity of metastasis detection can be improved via the kinetic parameter quantification and statistical signal detection.

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